Pediatric Nutritional Deficiencies: Case Presentations

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Disclosures

- We have no disclosures or financial affiliations

Objectives

- Identify pediatric patients at risk for nutritional deficiencies
- Evaluate and diagnose pediatric nutritional problems
- Treat various pediatric nutritional deficiencies
Introduction

- Our residency clinic is located in Grand Rapids, MI
- The clinic serves as a teaching center for family practice, internal medicine, OB/GYN, general surgery, orthopedics, and urology
- Our population consists of patients who are either uninsured or underinsured who otherwise have little to no access to care
- We additionally take care of a growing refugee population including those from central Africa, east Africa, southeast Asia, and Nepal

Case #1

- Patient is a 2 ½ year old Nepali male who presents to the clinic with his mother for a routine well child check
- The child has not been seen in over a year by one of our residents and will therefore be reassigned to me as the previous resident had graduated
- There is a Nepali interpreter present for the visit to assist with communication
- His mother's only concern is that her son has not been evaluated by a doctor in some time

Vitals

- BP 82/58
- HR 88
- RR 24
- Temp 98.2 F
- Ht 3' 2"
- Wt 34 lbs 9 oz
Growth/Development

• We begin our visit with a conversation about growth and development
• Based on the growth chart, the child appears to be following a predictable curve for both weight and height (75th percentile curve for weight and 75th percentile curve for height)
• He appears to be reaching all cognitive and physical milestones

Diet

• When asked about his dietary intake, his mother states that he is still breast feeding but eats a lot of “Nepali food” like his older family members
• Out of curiosity, I asked what constitutes “Nepali food,” which is a diet that mainly consists of rice, noodles, and beans
• Upon further questioning, he has rather limited intake of vegetables, fruits, or milk of any type

ROS

• During the review of systems, his mother notes that his legs are “crooked”
• His mother reports that for about the last year, both of his legs have taken on a bowed appearance
• He does not seem to be in pain and walks around the exam room without difficulty
• Remainder of the review of systems is unremarkable
Physical Exam

• Physical exam is notable for the following
  ▫ General: alert, non-cooperative and inconsolable with examination
  ▫ Neuro: cranial nerves II-XII grossly intact, reflexes normal in all extremities
  ▫ Musculoskeletal: free floating normal
  ▫ Eyes: extraocular movements intact and pupils reactive
  ▫ Ears: hearing intact and tympanic membranes are gray and shiny bilaterally
  ▫ Nose: nose with normal formation, lips and gingiva without lesions, tongue normal in appearance, palate intact
  ▫ Lungs: breath sounds clear to auscultation
  ▫ Cardiovascular: regular rate and rhythm without murmur
  ▫ Abdomen: abdomen soft, non-tender, bowel sounds active, no masses or organomegaly
  ▫ GU: normal phallic, normal scrotum and testes descended bilaterally, no hernias, no hydroceles
  ▫ Musculoskeletal: bilateral genu varus deformities of lower extremities with an intercondylar distance of 6-7 cm, subtle findings of a rachitic rosary noted at the costochondral junction, wrists appear widened
  ▫ Skin: skin warm and dry, no rashes or lesions

Assessment/Plan

• At this point, a provisional diagnosis of vitamin D deficiency rickets is assumed so labs were obtained (CMP, 25OHd, Phos, and PTH)
• X-rays of the extremities were not obtained as management would not be changed and due to the child’s lack cooperation with examination

Results

• Labs returned with the following abnormal values in red:
  ▫ CMP
    ▫ Ca 7.7 mg/dl (normal 8.5-10.1 mg/dl), Alk phos 871 U/L (normal 50-350 U/L)
  ▫ 25OHd
    ▫ 5 ng/mL (normal 30-100 ng/mL)
  ▫ PTH
    ▫ 112.9 pg/mL (normal 14.00 - 72.00 pg/mL)
  ▫ Serum phosphorus
    ▫ 3.4 mg/dL (normal 2.5-4.9 mg/dL)
Treatment plan

- Discussed case with one of our local pediatricians who recommended consultation with pediatric endocrinology
- Discussed case with specialist at HDVCH who recommended starting 8,000 IU of vitamin D2 daily in addition to 1250mg of calcium carbonate twice daily
- Recommended starting a children's multivitamin daily and increasing intake of dairy and vegetables
- Arranged follow-up with pediatric endocrinology for 3 months into treatment

Metabolism

- A quick review of vitamin D metabolism
- PTH functions as the main driver of calcium/vitamin D metabolism in the body
- Ultimately, activated vitamin D3 is necessary for the intestinal absorption of calcium
- Lack of vitamin D leads to low calcium and begins the release of PTH which is the pathophysiologic basis for rickets
- Recall that there are two basic components of bone, the osteoid portion formed of protein (collagen) and the mineralized portion consisting of calcium and phosphate
- When calcium is leached from the bones, the remaining osteoid is what remains

Etiology

- For the sake of time and relevance to this case, we'll discuss vitamin d deficiency (hypocalcemic) rickets
Diagnosis

- Thorough review of dietary intake
- Identify exam findings suggestive of the disease
- Radiographs of extremities are optional
- Laboratory workup
  - CMP (calcium/alk phos), serum phosphorus, PTH, 25OHD level, and urine calcium should be obtained
  - Classic rickets is identified by ↓ calcium, ↑ alkaline phosphatase, ↓ or normal serum phosphorus, ↑ PTH, ↓ 25 OHD level, and ↓ or normal urinary calcium

Physical exam

- Metaphyseal cupping/fraying
- Widening of the wrists

- Rachitic rosary

Prevention

- In the developed world we now fortify cereal, formula, and milk with vitamin D
- The American Academy of Pediatrics recommends supplementation for specific populations

Treatment

- For as complex of a disease as rickets seems, treatment is fairly straightforward
- Two basic treatment regimens exist
  - Daily supplementation
  - Stoss Therapy
- Oral calcium supplementation should occur simultaneously
- Follow treatment with biomarkers for disease

Follow-up

- 2 months into vitamin D and calcium treatment the patient presents for a follow-up visit in our clinic
- Patient’s mother explains that giving the medication via oral liquid has been somewhat difficult and that the child’s been spitting out some of the medication from time to time, but getting the majority of doses
- Child is examined again with the following significant finding...
Physical exam

- Angular cheilitis is noted with a similar appearance to previous photograph
- Formerly known as perlèche
- Review of the chart shows two prior visits for angular cheilitis a year ago
- Etiology was thought to be candidal and topical nystatin was prescribed
- History reveals that the lesions frequently come and go
- Rarely, angular cheilitis is caused by deficiencies of b vitamins or the micronutrients iron and zinc
- Back to the drawing board...

Results

- CBC
  - Hb 11.9 g/dL (normal 10.9-15.0 g/dL), MCV 73.5 fL (normal 75-95 fL), RDW 17.7% (normal 11.6-14.9%)
- Iron Studies
  - Ferritin 10.5 ng/mL (22-322 ng/mL), Serum iron 30 µg/dL (normal 65-175 µg/dL), TIBC 511 µg/dL (normal 250-450 µg/dL), % saturation of iron <10% (normal 20-50%)
- CMP
  - Ca 9.2 mg/dL (normal 8.5-10.1 mg/dL), Alk phos 423 U/L (normal 50-350 U/L)
  - 25OHD
    - 47 ng/mL (normal 30-100 ng/mL)
- PTH
  - 71.40 pg/mL (normal 14-65 pg/mL)
  - Serum phosphorus
    - 5.5 mg/dL (normal 2.5-4.9 mg/dL)
Conclusion

- Vitamin D supplementation was converted from high-dose oral therapy to a maintenance dose of 2,000 units of vitamin D3 daily in chewable form
- Recommended continuation of daily multivitamin
- Recommended starting oral iron therapy
- At 6 month follow-up, skeletal deformities were still present but improved significantly

Case #2

- 2 ½ year old female presents with mother for well child visit
- Last well child visit about 13 months prior but had been seen for sick visits by other providers who were not the PCP
- Patient reassigned to me since previous PCP left
- Upon chart review: microcytic anemia and started on PO ferrous sulfate
- Mother was instructed to bring patient in for repeat CBC in one month with appointment to follow
- Patient was drinking 6 cups of whole milk per day at 15 months old → 48 ounces
- Mother educated to decrease milk consumption and given "Age-by-Age Feeding Guide" that was reviewed at the visit
CSC | CSC (continued)  
---|---
WBC (K/µL) | 5.4 | Reactive lymphocytes % 1  
RBC (Million/µL) | 4.44 | Microcyte 2+  
Hemoglobin (g/dL) | 10.6 | Platelet morphology Normal  
Hematocrit (%) | 32.5 |  
MCV (fL) | 73.1 | Hemoglobin at 12 months 9.8  
MCH (pg) | 23.9 |  
MCHC (g/dL) | 32.7 | Lead <3.3  
RDW (%) | 15.1 |  
Platelet count (K/µL) | 415 | Retic count (0.50-2%) 1.70  
Neutrophil ABS (K/µL) | 0.6 | Retic absolute (21.0-77.0 K/µL) 73.3  
Neutrophil % | 11 |  

Labs from 15 month well child visit

Case #2

**Vitals**
- HR 98
- RR 20
- Temp 36.6 °C (97.8 °F)
- Height 0.927 m (3' 0.5")
- Weight 15.025 kg (33 lb 2 oz)

**Growth/Development**
- Weight 90th percentile
- Height 83rd percentile
- Following predictable curve for growth and meeting milestones

**Diet**
- Eats some veggies, fruit, and meats but tends to be very picky
- Drinking 1 gallon of 2% milk daily = 128 ounces daily!!!
- Does not take a multivitamin and never started ferrous sulfate from previous visit
- Mother states that she cries for hours until you give her milk and refuses to take much other food
- Drinks 4-8 oz juice and water daily
ROS

- ROS negative except mother reports she was recently treated in ED for hand, foot, and mouth but has had complete resolution of her symptoms.

Physical exam

- Full physical unremarkable except for generalized pallor

Assessment/Plan

- Well child visit
- Neutropenia
  - Referral to Pediatric Hematology/Oncology
  - CBC with diff
- Iron deficiency anemia
  - CBC with diff
  - TIBC & iron with % saturation
  - Ferritin
  - Peripheral blood smear
  - Lead
### Results

<table>
<thead>
<tr>
<th>CBC</th>
<th>CBC (continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (K/uL)</td>
<td>2.6</td>
</tr>
<tr>
<td>RBC (Million/uL)</td>
<td>4.46</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>8.3</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>25.7</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>57.7</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>18.6</td>
</tr>
<tr>
<td>MCHC (g/dL)</td>
<td>32.6</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>18.5</td>
</tr>
<tr>
<td>Platelet count (K/uL)</td>
<td>359</td>
</tr>
<tr>
<td>Neutrophil ABS (K/uL)</td>
<td>0.1</td>
</tr>
<tr>
<td>Neutrophil %</td>
<td>5</td>
</tr>
</tbody>
</table>

- **Peripheral blood smear**
  - Microcytic, hypochromic anemia and neutropenia
  - Erythrocytes: Marked anisocytosis, hypochromasia, polychromasia, occasional teardrop cells, and acanthocytes
  - Leukocytes: Decreased, rare granulocytes
  - Platelets: Unremarkable

### Treatment

- Prescribed patient ferrous sulfate and called Pediatric hematology and oncology at Helen Devos Children’s Hospital
- Due to the associated neutropenia, hematology planned to see patient in the office the next day
Discussion of Iron deficiency anemia

• Why should we care about iron deficiency anemia in our children?
  ▫ Has been associated with impaired neurocognitive function in infants, which can be irreversible (studies in Costa Rica and Chile)
  ▫ Iron is necessary for myelination of neurons, differentiation of brain cells, and as a cofactor for enzymes that synthesize neurotransmitters
  ▫ Some studies cite possible cerebral vein thrombosis, breath holding spells, increased risk of seizures, and restless leg syndrome as an adult
  ▫ Can also lead to pica, pagophagia, and plumbism
  ▫ Effects on immunity and infection are mixed

Definitions

• Anemia: hemoglobin concentration 2 standard deviations or more below the mean for same gender (after age 12) and age
  ▫ Thresholds from the WHO
    ◆ 6 months to <5 years: 11 g/dL
    ◆ 5 to <12 years: 11.5 g/dL
    ◆ 12 to <15 years: 12 g/dL
  ▫ Iron deficiency: iron insufficiency to maintain normal physiologic functions, ferritin <12 mcg/L in children <5 yo and <15 mcg/L in children >5 yo in the absence of conditions that can change ferritin levels

Epidemiology

• Rate of infant and childhood anemia low (about 7-9%) in US but low-income children have the highest prevalence at 18.2% among children 12 to 17 months old
• Black and Hispanic children most commonly affected
• Worldwide IDA is much higher in non-developed countries
  ◆ Africa, Latin America, and Southeast Asia have high prevalence of anemia at 45-65 % of children with about half due to iron deficiency
Risk factors for IDA

- Childhood obesity
- Prematurity or low birth weight
- Perinatal risk factors
- African-American and Hispanic children living in poverty
- Immigrant status
- Early cord clamping
- Menstruation in adolescent females
- Dietary factors (next slide)
- Gastrointestinal
  - IBD, cow’s milk protein-induced colitis, chronic NSAID use, celiac disease, Crohn disease, meckel diverticulum, hemangioma, giardiasis, H pylori, hookworm, and resection of the proximal small intestine

Dietary risk factors for IDA

- Intake of foods that are insufficient in iron
- Decreased intestinal absorption due to the types of dietary iron and other foods ingested (can be problematic in vegetarians)
- Use of non formula cow’s milk before 12 months of age
- GI occult blood loss due to colitis from cow’s milk protein
- Ingestion of >24 ounces cow’s milk per day

Pathophysiology

- Iron
  - Essential nutrient
  - 75% bound in heme proteins, hemoglobin, and myoglobin
  - Typically only a small amount enters and leaves the body daily
  - Recycled from breakdown of old RBCs by macrophages
  - Infants and children consume about 30% of daily iron needs from their diet compared to adults consuming about 5%
- Absorption in the GI tract is influenced by:
  - Stores (transferrin and ferritin)
  - Bioavailability of iron from diet
  - Erythropoietic rate
Pathophysiology
• Low iron stores and increased or ineffective erythropoiesis → increased GI absorption
• Stores depleted (reduced serum ferritin) → serum iron levels decrease → TIBC increases → transferrin saturation decreases → cannot form heme and hemoglobin synthesis impaired → RBCs become smaller and vary in size (increased RDW) → decreased MCV and MCH
• Infants maintain their iron stores from birth for the first 6-9 months

Clinical manifestations
• Usually asymptomatic and identified by screening
• Those with severe anemia:
  ▫ Pallor of conjunctivae, palms, palmar creases, and nails beds; irritability; lethargy; poor feeding; cardiomegaly; systolic flow murmur, and tachypnea
• Pt may present with GI disease
• Neurodevelopmental changes as noted previously
  ▫ Thought that it may contribute to ADHD

Screening
• AAP and WHO: universal screening at age 1 and AAP recommends selective screening in children at any age if concern due to risk factors
• Risk assessment based on dietary history and review of risk factors at 4, 15, 18, 24, 30 months, 3 years of age and annually thereafter.
• USPSTF did not find sufficient evidence to evaluate the benefits vs harms of screening
• CBC is most common initial screening and minimum is a hemoglobin
  ▫ For children with significant risk factors may obtain ferritin (acute phase reactant) during initial screen and CRP can be considered
Differential diagnosis

- Poor compliance (true intolerance of Fe is uncommon)
- Incorrect dose or medication
- Malabsorption of administered iron
- Ongoing blood loss, including gastrointestinal, menstrual, and pulmonary
- Concomitant infection or inflammatory disorder inhibiting the response to iron
- Concomitant vitamin B₁₂ or folate deficiency
- Diagnosis other than iron deficiency
  - Thalassemias
  - Hemoglobin C and E disorders
  - Anemia of chronic disease
  - Lead poisoning
  - Sickle thalassemias, hemoglobin SC disease
  - Iron refractory iron deficiency anemia (IRIDA)
  - Rare microcytic anemias

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Treatment

- PO ferrous sulfate is effective and inexpensive however poor taste
  - Young children do not typically have GI complaints seen in older children and adolescents
- Ferrous sulfate dosed in terms of elemental iron
  - 3-6 mg/kg elemental iron in 2-3 divided doses, max 150-200 mg
  - Ideally given with juice in between meals
- IV preparations only necessary when malabsorption is present or poor compliance with PO

Dietary counseling/Follow-up

- Cow milk consumption should be less than 20-24 oz daily in children aged one to five
- Repeat blood count about 1 month after start of treatment
- Treatment should be continued for 2-3 months after labs normalize to replace iron stores
- If poor response to treatment must consider other diagnosis or non compliance
- Blood transfusions only necessary in severe cases with ongoing blood loss or heart failure

Response to treatment

<table>
<thead>
<tr>
<th>TIME AFTER IRON ADMINISTRATION</th>
<th>RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-24 hr</td>
<td>Replacement of intracellular iron enzymes; subjective improvement; decreased irritability; increased appetite</td>
</tr>
<tr>
<td>48-72 hr</td>
<td>Initial bone marrow response; erythroid hyperplasia</td>
</tr>
<tr>
<td>4-30 days</td>
<td>Reticulocytosis, peaking at 7-10 days</td>
</tr>
<tr>
<td>1-3 mo</td>
<td>Increase in hemoglobin level</td>
</tr>
<tr>
<td>1 yr+</td>
<td>Repletion of stores</td>
</tr>
</tbody>
</table>

Recommended dietary allowances

- Full term infant: 1 mg/kg daily (max 15 mg)
- Premature infants: 2 to 4 mg/kg daily (max 15 mg)
- 1 to 3 years old: 7 mg daily
- 4 to 8 years old: 10 mg daily
- 9 to 13 years old: 8 mg daily

Prevention

Breastfed infants need iron supplementation

- Full term infants start elemental iron at four months old 1 mg/kg daily (max 15 mg)
- Premature infants start elemental iron at two weeks old 2-4 mg/kg daily (max 15 mg)
- Infants younger than 12 months who are not breastfed should have iron-fortified formula with 12 mg/L of iron
  - AAP recommends against low-iron infant formula (<6.7 mg/L)

Prevention-Dietary recommendations

- 6 months old: intake of vitamin C rich foods and consider pureed meats if developmentally ready
- Avoid cow’s milk until 12 months old
- Children one to five years old should limit milk intake to 18-24 oz daily
- If child consumes < three servings of iron-rich foods daily, may need iron supplement
Iron Content in Common Foods

<table>
<thead>
<tr>
<th>Food (serving size)</th>
<th>Amount of elemental iron (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybeans: cooked (1/2 cup)</td>
<td>4.4</td>
</tr>
<tr>
<td>Lentils: cooked (1/2 cup)</td>
<td>3.3</td>
</tr>
<tr>
<td>Spinach: cooked/boiled, drained (1/2 cup)</td>
<td>3.2</td>
</tr>
<tr>
<td>Beef: cooked (3 oz)</td>
<td>2.5</td>
</tr>
<tr>
<td>Beans (lima, navy, kidney, pinto): cooked (1/2 cup)</td>
<td>1.8 to 2.2</td>
</tr>
<tr>
<td>Baby food brown rice cereal: dry (1 tbsp)</td>
<td>1.8</td>
</tr>
<tr>
<td>Baby food green beans (6 oz)</td>
<td>1.8</td>
</tr>
<tr>
<td>Baby food oatmeal cereal: dry (1 tbsp)</td>
<td>1.6</td>
</tr>
<tr>
<td>Turkey and chicken: dark meat (3 oz)</td>
<td>1.1 to 2.0</td>
</tr>
<tr>
<td>Baby food lamb or chicken (2.5 oz)</td>
<td>1.2 to 1.5</td>
</tr>
<tr>
<td>Baby food peas (3.4 oz)</td>
<td>0.9</td>
</tr>
</tbody>
</table>


Back to Case #2...Evaluation by Hematology

• Hemolysis and celiac disease were ruled out with labs
• Given patient’s milk consumption the diagnosis of iron deficiency anemia is supported
  ▫ Since MCV disproportionately low and reticulocyte count high may have underlying thalassemia but will replace iron stores first
  ▫ Patient prescribed NovaFerrum 15 mg elemental iron/1 ml, take 2 ml BID=4 mg/kg/day elemental iron
  ▫ Recommended to decrease milk consumption to <16 oz per day
• Her neutropenia was found to be autoimmune related and she was placed on Neupogen

Conclusion

• The patient did not follow-up with hematology due to a lapse in insurance and when seen her labs were not improved as expected on PO iron due to multifactorial non-compliance secondary to financial reasons, maternal misunderstanding, and difficulty with administration
• Anemia corrected after 4 weeks of IV iron and then placed on NovaFerrum 3 mg/kg/day PO
• Hemoglobin fractionation was normal and alpha-globin gene analysis was normal
• Continued to have anemia but Hgb stable at 10, consider bone marrow evaluation to look at iron stores in 4-6 months
References